SCIENTIFIC REVIEW - COMMENTS

GuLF Worker Study:

Gulf Long-Term Follow-Up Study for Oil Spill Clean-Up Workers and Volunteers

September 20, 2010

Reviewer Comment	Investigator Response
Reviewer #1	
Soundness of Experimental Design: 1) The ability to enumerate those eligible for the study is quite challenging. While the plans call for using multiple sources, it is not clear how confidently they will ultimately be able to provide denominators for the cohort that is enrolled.	Almost all workers were required to undergo safety training prior to engaging in clean-up activities. While the training for most individuals is recorded on the Petroleum Education Council (PEC) list, some workers underwent separate training through their governmental agency or, for a handful of communities, through their local parish. We plan to obtain all such lists, which should allow us to make a very good determination of the denominator of the worker population. We plan to additionally obtain the lists of persons issued badges, which were required for entry into the clean-up staging areas. We are also working to obtain the BP payroll lists for clean-up workers. To address the possibility that some workers may not be on the above lists because of language or cultural barriers, we are developing scientifically valid strategies for working with community groups and professional organizations (e.g., shrimpers associations) to identify such workers and recruit them into the study. We have begun meeting with these groups to get their feedback on the planned study and to enlist their active support. Thus, we anticipate a comprehensive enumeration of the worker population through these diverse but overlapping sources.
2) The inclusion of unexposed controls is a logical goal but one that may be achieved in other ways or may not be fully attainable	We agree that exposure-response analyses that compare highly exposed workers to low-exposed workers will be

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at all.	particularly important and is readily achievable in this study. We plan to oversample more highly exposed workers and will have a substantial number of low exposed workers, facilitating such analyses. A valuable function of an unexposed control group, particularly one away from the immediately affected areas, is to allow us to assess health outcomes associated with the psychological and financial stresses related to the spill, which will be likely be shared by most, if not all, clean-up workers. We are attempting to address the healthy worker effect by including in the enrollment questionnaire questions intended to distinguish, to the extent possible, between persons who were trained but not hired because of pre-existing health conditions vs. those who were not hired simply because they were not needed.
3) The team of investigators is outstanding, but represents more general expertise in occupational and environmental epidemiology. There are a few realms that call for a more prominent presence, whether through collaboration or consulting: a) Mental health epidemiology,	We are in the process of enlisting co-investigators and consultants with the necessary expertise in specific areas, including industrial hygiene, exposure assessment, toxicology, mental health, neurology, immunology, social epidemiology, GIS/meteorology and statistics. We are especially focusing on industrial hygienists, exposure assessment experts, and toxicologists with expertise in petrochemical exposures.
Feasibility of the Objectives: 1) For the clinical examinations, sampling might be done in part based on geographic proximity to medical centers in the Gulf coast area, i.e., within X miles of specific centers. This would do no harm to the validity of the results and ease the travel for those	For the active follow-up cohort, we propose to conduct the baseline examination in their homes to ease the travel burden on the participant. We are currently working with state and local health officials, and community groups to determine whether other locations for data collection would

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who participate.	foster better participation and increased convenience for those who participate.
2) Plans may need to be made to respond to those who were otherwise ineligible but volunteer to be in the study – reconciling the public relations and scientific issues when such calls are received.	Inclusion of ineligible subjects could introduce bias into the study depending on their motivation for wanting to participate. As suggested, we will develop strategies for dealing with this issue.
3) The tight time-line limits pilot testing to a worrisome degree but may be insurmountable. Some time to make sure that the questionnaire includes all common concerns of the community is needed, whether through formal focus groups or some less structured means.	Because of time constraints, this issue is currently being addressed informally through meetings with community and worker groups. In addition, the questionnaires will be posted online and distributed for feedback prior to going into the field.
4) The value of home environmental samples is not entirely clear, depending on the time frame they reflect and how much of a contribution those exposures would have to total exposure. While there will be the usual generic in-home exposures to pesticides, etc., the need to address those in this study is not obvious.	The Gulf community contains a large number of petrochemical plants and other sources of ongoing exposures relevant to this study. The protocol includes collection of home environmental samples in order to determine general levels of such exposures, which could otherwise confound estimates of associations between clean-up work and disease.
Reviewer #2	
Feasibilty of the Objectives: 1) The biggest challenge will be exposure reconstruction; especially since many/most compounds of interest will not persist, or will not be easily detected on biomarker testing long after exposure. The approach proposed in [sic] the best possible,	An expert panel will be convened to address this issue. We will address exposure reconstruction by incorporating data and information from multiple sources. Exposure reconstruction will be based on the large amount of area and personal monitoring data collected by various government agencies and by BP, together with toxicology data, meteorological data, environmental data on the

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	dispersion of the oil, health hazard evaluations, qualitative and quantitative exposure data from previous oil spills, and expert judgment. We plan to use these data sources, combined with self-reported activity levels and validated tasks/location information (e.g. security badge access records, timecards, payroll records, etc. where available) to develop job-exposure matrices (JEMs) that will allow us to estimate individual exposures by task, time, and place. Such JEMs have been successfully used in many previous epidemiologic studies. Biomarkers of exposure will be used only for compounds such as metals that are accurately measurable given the planned timing of specimen collection relative to clean-up related exposure.
Reviewer #3	
Feasibility of the objectives 1) The planned study population is appropriate. My one reservation about the population has to do with the federal control group. Have these employees been involved in other oil spill or hazardous materials cleanup efforts to an extent that differs from the federal employees who participated in the current cleanup? Perhaps some thought could be given to the matching the federal controls to the exposed federal workers. The subject inclusion/exclusions are reasonable.	The magnitude of the Deepwater Horizon spill is unprecedented, and the extent of the mobilization of Federal workers is expected to be similarly so. As the protocol now indicates, we will determine from the participating agencies the extent to which this is an issue and will select Federal controls accordingly. The questionnaires will include a section on past occupational and recreational (hobbies) exposures to petroleum and petroleum based products to help differentiate those with prior exposure to other oil spill or hazardous materials cleanup efforts.
Human Subjects Consideration 1) Interviewers will be collecting data in the field on laptop	All data will be encrypted on the laptops and will be securely transferred using standard technical protocols, as clarified in

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computers and transferring the data by phone to a central database. More details should be provided that describe how the data will be secured on the laptops, during data transfer, and at the central database. Training for interviewers and their supervisors should also include confidentiality and security of the data.	the latest version of the study protocol. The training manuals and operations manuals will also include these data security details and procedures to ensure adequate human subjects protections are in place and followed.
Reviewer #4	
Soundness of the Experimental Design 1) The infrequency of contacts in the Active group may not be optimal for long-term participant retention.	We will implement multiple strategies for minimizing loss-to-follow-up among the Active Follow-up Cohort, which is important for the validity of the study. Members of this cohort will be administered a telephone interview in Years 2 and 4 of the study, and possibly in years in Years 6-7 and 9-10 depending on availability of funding and study findings to date. All study participants, including those in the Active Follow-up Cohort, will be asked to complete a one-page update form annually, whether or not they have had any changes in their contact information. Any mailings that have been "returned to sender" will undergo tracing to identify updated address information. These annual mailings, together with the biennial telephone interviews, will allow us to track changes in address and minimize losses to follow-up. We will send reminder post-cards to participants who do not return the annual follow-up form.
2) The timing of this study's implementation might not be ideal, in that the large bulk of the oil spill cleanup work may be complete by the time of study participant enrollment.	Delays in collecting exposure and health outcome data are an inevitable part of disaster epidemiology, given the unpredictability of disasters. Nonetheless, studies of previous disasters, including the WTC, Prestige oil spill, Chernobyl, Bhopal, and Seveso, all produced valuable

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	public health and scientific information, albeit with the limitations that result from the inability to plan such studies in advance and the need to respond both quickly and effectively after they occur. The limited epidemiologic literature on oil spills, especially that of the Prestige oil spill, which is the best and longest studied to date, indicates that health effects can be observed up to two years after the event. While some misclassification of acute health effects is expected, given the delay in starting data collection, previous studies suggest that we will still observe such effects if data collection begins soon, as is planned. However, subject recruitment will begin in time to investigate the short-term and long-term health effects that are a major focus of this study and for which there is a dearth of scientific literature.
3) While these timing concerns are fundamental to the investigation of an exposure that may have already largely occurred, there are scientific risks to developing key aspects of the study (e.g., exposure and outcome measures, hypotheses and aims) while the study is ongoing.	Although the development and evaluation of job-exposure matrices for the present worker population would ideally have been done prior to beginning subject recruitment, this was not a feasible option for this study, as is typically the case for studies responding to disasters. We have consulted individually with researchers who examined health effects associated with past oil spills and we are exploring the possibility of convening an exposure assessment workshop of all of these investigators to explore lessons learned and to discuss findings to ensure that the GuLF Worker Study is conducted to the state-of-the-science. Importantly, a large amount of area and personal monitoring data has already been collected, is currently being aggregated, and will be available to us. Our main concern to this point has been to design a scientifically rigorous study as quickly as possible

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	so that we can get into the field as quickly as possible and 1) capture the self-reported activities, dates, times, locations, etc. of clean-up work that these workers engaged in before their memories fade and 2) enroll these workers into the study before they move, change phone numbers, or otherwise become lost to follow-up. These issues have been clarified in the protocol.
4) They will construct job-exposure matrices for the exposures of interest using monitoring data from multiple sources (e.g., exposure questionnaires, house dust, tap water, chemical analysis data from the leaking oil well, weather data). How this can come together to provide meaningful, valid exposure measures is unclear and untested.	It is important to note that many scientifically rigorous epidemiologic studies have successfully used qualitative and semi-quantitative data derived from job-exposure matrices to investigate exposure-disease associations. Indeed, the epidemiologic investigations surrounding the *Prestige* oil spill response in Spain utilized self-reported exposure information to assess health outcomes that otherwise might have been missed. Such studies have yielded scientifically valuable information and demonstrate the important role that semi-quantitative exposure data and/or job-exposure matrices can play in epidemiologic research.
5) The secondary and sub-study objectives, to develop a valuable resource for collaboration, and for a biological cohort with multiple clinical and biological assessments of the study participants, can lead to innovative, high impact research. This has largely not been developed, specified, or budgeted; the likelihood of success is accordingly undeterminable.	The secondary and substudy objectives, including examination of special populations as well as biomarkers of effects, are described in limited detail in the protocol only to illustrate the *types* of studies that will be possible and to put into context the steps that we have taken to maximize the potential utility of this cohort for public health investigations related to oil spills. We have prioritized getting into the field as quickly and scientifically rigorously as possible to collect the necessary data, biospecimens, and environmental samples, without which the secondary and substudy objectives would not be possible. These objectives will be

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	further developed based on available funding and local collaborators, and will undergo separate IRB review.
6) It is difficult to critically determine if the proposing investigators are trained and well suited for this investigation because no investigator biosketches, specific roles and responsibilities, or support letters were included.	As described above, under Reviewer 1, we are in the process of enlisting co-investigators and consultants with the necessary expertise in specific areas, including industrial hygiene, exposure assessment, toxicology, mental health, neurology, immunology, social epidemiology, and statistics, with a focus on persons with expertise in petrochemical-related exposures. We will also be providing biosketches of the listed investigators in an update to this protocol document.
7) Without specific aims and hypotheses based on prior research, the power calculations do not justify the proposed study participant numbers.	There have been very few published studies of the health effects associated with oil spills. Almost all of these studies have been cross-sectional. This study is exploratory in that the literature on short-term health effects is very limited (and very short-term) and the literature on long-term physical effects is nonexistent. Consequently, we have presented power calculations that cover a wide range of exposure and outcome distributions. As shown in the current protocol, this study is well powered to identify the acute- and short-term health effects observed in the few other epidemiologic studies of oil spills and also to examine a range of other, relatively rare outcomes.
8) It may be helpful to consult the IRB about potential HIPPA issues in the recruitment strategy (directly from worker and volunteer lists) and 'indefinite' sample storage, considering the different institutions, organizations, and states involved in	The NIEHS IRB will review all aspects of this protocol, including consent, HIPAA concerns, remuneration, and recruitment strategies. NIH is covered by the Privacy Act rather than HIPPA per se, though protections provided

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this study.	under both are similar. We have worked with the NIH Office of General Council to develop appropriate data sharing agreements to obtain access to worker lists. The agreements take into account relevant privacy and HIPPA issues of the organization providing those lists. We have further consulted with Privacy Act and HIPPA experts at NIH as we developed the study plans. State Health Departments and other State groups have been consulted about recruitment strategies. To the extent that other collaborating institutions become involved in primary data collection and/or storage, those institutions will require local IRB oversight.
Chairperson Summary	